



Prostate Cancer

The Optimal Rebiopsy Prostatic Scheme Depends on Patient Clinical Characteristics: Results of a Recursive Partitioning Analysis Based on a 24-Core Systematic Scheme

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Article info

Article history:

Accepted July 8, 2011

Published online ahead of print on July 30, 2011

Keywords:

Prostatic neoplasms
 Prostate biopsy
 Diagnosis
 Transrectal ultrasound

Abstract

Background: The most beneficial number and the location of prostate biopsies remain matters of debate, especially after an initial negative biopsy.

Objective: To identify the optimal combination of sampling sites (number and location) to detect prostate cancer (PCa) in patients previously submitted to an initial negative prostatic biopsy.

Design, setting, and participants: A transrectal ultrasound-guided systematic 24-core prostate biopsy (24PBx) was performed prospectively in 340 consecutive patients after a first negative biopsy (at least 12 cores).

Measurements: We relied on a classification and regression tree analysis to identify three clinically different subgroups of patients at dissimilar risk of harboring PCa at second biopsy. Subsequently, we set the cancer-positive rate of the 24PBx at 100% and calculated PCa detection rates for 255 possible combinations of sampling sites. We selected the optimal biopsy scheme (defined as the combination of sampling sites that detected 95% of all the cancers with the minimal number of biopsy cores) for each patient subgroup.

Results and limitations: After an initial negative biopsy, cancer was detected at rebiopsy in 95 men (27.9%). At a given number of cores, the cancer detection rates varied significantly according to the different combination of sites considered. Three different PCa risk groups were identified: (1) previous report of atypical small acinar proliferation of the prostate (ASAP), (2) no previous ASAP and ratio of free prostate-specific antigen (fPSA) to total PSA (%fPSA) $\leq 10\%$, and (3) no previous ASAP and %fPSA $> 10\%$. For patients with previous ASAP or patients with no previous ASAP and %fPSA $\leq 10\%$, two schemes with different combinations of 14 cores were most favorable. The optimal sampling in patients with no previous ASAP and %fPSA $> 10\%$ was a scheme with a combination of 20 cores.

Conclusions: Both the number and the location of biopsy cores taken affect cancer detection rates in a repeated biopsy setting. We developed an internally validated flowchart to identify the most advantageous set of sampling sites according to patient characteristics.

Published by Elsevier B.V. on behalf of European Association of Urology.

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1. Introduction

Patients with a prior negative prostate biopsy but a persistent suspicion of prostate cancer (PCa) on the basis of abnormal digital rectal examination (DRE), prostate-specific antigen (PSA) measurements, and histologic findings, namely, atypical small acinar proliferation of prostate (ASAP) and high-grade prostatic intraepithelial neoplasia (HGPIN), should be considered for a repeated biopsy [1]. Because initial 10- to 12-core biopsy schemes may miss almost a third of cancers [1,2], a saturation prostate biopsy (SPBx) has been adopted to improve PCa detection rate in the repeat setting. Several authors showed that SPBx increases the detection rate of PCa in patients with suspicious clinical findings following previous negative standard prostate biopsy compared with repeat standard biopsy strategies using up to 12 cores [1–6].

Nevertheless, the most efficient scheme with the optimal number and location of the cores has not yet been defined [1]. It is not clear whether it is critical to perform the same sampling protocol in each patient or to modify the protocol according to the different clinical parameters, such as PSA value, DRE findings, or prostatic volume [7]. It is still contentious whether the detection rate may vary simply with additional biopsies or it is due to the different locations from which the cores are taken [1,2,4].

We evaluated cancer detection rates on an individual-core basis after a 24-core prostate biopsy (24PBx) and investigated the ability of various biopsy regimens, which are characterized by the number and anatomic location of cores taken, to detect PCa. We also attempted to identify the optimal number and location of the cores to detect the maximum number of PCas with the minimum number of cores according to different clinical parameters.

2. Patients and methods

2.1. Procedure

Following institutional review board approval, from September 2005 to June 2008 we prospectively performed a saturation 24PBx in 340 consecutive patients suspected of harboring PCa after a first negative biopsy sampling (at least 12 cores taken) [8]. The indications to perform a rebiopsy were PSA >4.0 ng/ml and/or abnormal DRE ($n = 229$) and/or initial HGPIN ($n = 78$) or ASAP ($n = 33$). Five dedicated urologists performed the procedures during this period.

Each physician used a TRUS (transrectal ultrasound) end-fired probe at a variable frequency of 5–7.5 MHz to guide the 18-gauge transrectal needle for prostate biopsy. SPBx was done on an outpatient basis using topical prilocaine-lidocaine cream combined with a peripheral nerve block that included the endorectal injection of 5 ml lidocaine (2%) bilaterally [9,10].

The biopsy patterns targeted six sectors (apex, lateral, and base, bilaterally) and the transition zone (TZ) to ensure a broad sampling area (Fig. 1). Three or four cores were taken from a specific zone of the sector for a total of 24 cores, and each single core was individually marked. The scheme (Fig. 1) consisted of the overlapping of the classical sextant scheme of Hodge (white points), the more lateral sextant scheme of Stamey (black points), eight more lateral and subcapsular cores (blue-green points), and four cores from the TZ [2]. The 24 cores were immediately put on sponge

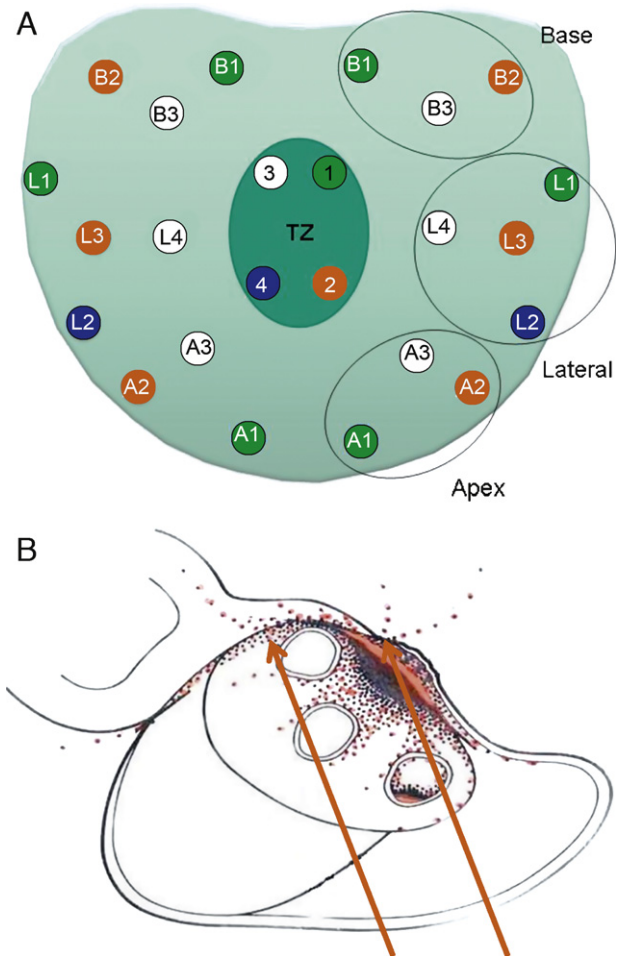


Fig. 1 – The figure shows the exact position of the 24 cores. The white cores belong to the classic Hodge scheme, the black cores to the Stamey scheme, and the blue-green cores to the more lateral and subcapsular cores. The number on the core represents the exact sequence and order of how the cores were taken and put in the sponge tissue on the sandwich cassette. The figure also shows the three sectors (apex, lateral, and base) and the transition zone from which the cores were taken and the colors used to mark each single core on the cassette (black, green, and blue). We started from the right lobe to the left lobe, from the apex to the base (A, apex; L, lateral; B, base). (A) Two transition zone (TZ) cores (No. 2 and No. 4) were directed through the adenomas to the anterior capsule; the other two posterior TZ cores were directed into the adenoma. (B) The arrows show the direction and the position of the biopsies in each lobe.

tissue in seven different sandwich cassettes and individually inked with different colors to mark the sites from which they were collected [11]. All slides were reviewed by a single experienced uropathologist (MF) using contemporary diagnostic criteria for HGPIN, ASAP, and PCa.

2.2. Statistical analysis

One-way analysis of variance and chi-square analyses were used to compare means and proportions, respectively. The sextant scheme of Stamey was set as the baseline. We added one single core from each side of the prostate, and we calculated the cancer detection rates for each scheme with 8, 10, 12, 14, 16, 18, 20, and 24 cores (considering all the biopsies of the TZ taken together). A total of 255 possible combinations were created, based on the sites of the cores. Because the exact prevalence of cancer cannot be assessed, to define how many cancers

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